

ARGUMENTS

I. Rejection of claims 1-5, 14-17, and 21-22 under 35 U.S.C. §103 as obvious over U.S. Patent No. 5,374,657 to Kyle in view of Crozier, G.L., et al., (Monatschrift Fur Kinderheilkunde, Vol. 143, No. 7, 1995, page 95-98) and Schweikhardt, et al.

The Examiner rejected claims 1-5, 14-17, and 21-22 under 35 U.S.C. § 103(a) as being obvious over Kyle in view of Crozier and Schweikhardt. The Examiner asserted that Kyle teaches an infant formula comprising DHA and ARA and that the presence of those two fatty acids in infant food is critical for the “healthy growth” of the infants. Admitting that Kyle does not teach the administration of that infant formula to preterm infants, the Examiner then asserted that Crozier, *et al.* teach that “the presence of ARA and DHA in food is particularly important for the proper growth and development of preterm infants because they are unable to synthesize sufficient ARA and DHA.” The Examiner also admitted that while both Kyle and Crozier fail to teach or suggest the amounts of ARA and DHA now claimed, Schweikhardt discloses such amounts. Thus, the Examiner concluded that it would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to administer the infant formula of Kyle to the preterm infants of Crozier in the amounts suggested by Schweikhardt.

Even if one of ordinary skill in the art were to combine Kyle, Crozier and Schweikhardt, a combination that Applicants contend is not suggested by the prior art, the combination would still not teach or suggest every one of the limitations in the amended claims of the present application. See MPEP § 2142 - § 2143 (explaining that the prior art references, when combined, must teach or suggest all the claim limitations); and see *In re Royka*, 180 U.S.P.Q. 580 (C.C.P.A. 1974) (“All words in a

claim must be considered in judging the patentability of that claim against the prior art.”). Specifically, the combination of Kyle, Crozier and Schweikhhardt does not teach or suggest a method for enhancing the weight gain of preterm infants by administering to the preterm infants a weight gain enhancing amount of DHA and ARA as required by the amended claims of the Application.

The current amendments to the claims, replacing the terms “physical growth” with “weight gain” are supported by the specification and do not introduce new matter into the application. It is clear to one skilled in the art that the application measures growth in terms of weight gain, as indicated, for example, on page 14, lines 15-16. The “Criteria for Response” in the study includes “[g]rowth as measured by weight achieved at 48 and 57 weeks postconceptual age comparable to formula control group.” *Id.* Similarly, the specification sets forth that “[w]eight gain during hospitalization was no less on D or DA than on C.” Page 19, lines 30-31. Thus, the present amendments are fully supported in the application disclosure.

The Examiner states that Kyle teaches the presence of DHA and ARA in infant food is critical for the “healthy growth” of infants. Likewise, the Examiner states that Crozier teaches that the presence of ARA and DHA in food is particularly important for the “proper growth and development” of preterm infants because they are unable to synthesize sufficient ARA and DHA.

Crozier, however, teaches “proper growth and development” in terms of nerve tissue. On page 96, lines 1-22, Crozier explains:

Both docosahexaenoic and arachidonic acids are important in brain growth. Brain tissue is 60% lipid and its fatty acid composition is surprisingly constant: the predominant acids are AA [ARA] and DHA.

On page 97, column 2, lines 1-21, Crozier discusses the apparent effect of these fatty acids on visual function and brain development:

Breast feeding has an effect on maturation of visual acuity. Measures of visual evoked potential and forced-choice preferential looking were significantly different in infants fed breast milk compared to those fed formula. Measures of intellectual development have also been demonstrably different between breast and formula fed preterm infants. Morley et al. showed that preterm infants who had been given breast milk had better developmental scores at the age of 18 months. This advantage continued; at 7.5 to 8 years of age, the breastfed group scored significantly higher intelligence quotients as determined by the Weschler Intelligence Scale for Children.

This clearly shows that for Crozier, “proper growth and development of the preterm infants” means proper growth of the nervous system and mental development of the preterm infant. Preterm infants’ proper brain growth, accelerated maturation of visual acuity, and improved intellectual development are the benefits that Crozier seeks in promoting the addition of DHA and ARA to preterm infants’ formula. Crozier simply does not teach or suggest enhancing the weight gain of preterm infants by administering to them a formula containing a weight gain enhancing amount of DHA and ARA.

The Examiner did not find Applicant’s argument that Crozier teaches away from the present invention persuasive. The Examiner states that Crozier, as a whole, “suggests the administration of a combination of DHA and AA to provide benefit to preterm infant.” The present invention provides DHA and ARA to enhance the weight gain of a preterm infant, not merely to “provide benefit to preterm infant.”

In fact, Crozier does teach away from enhancing the weight gain of preterm infants. Crozier suggests that the addition of ARA be made for purposes other than for compensating for the drop in weight gain caused by DHA in the Carlson study.

Specifically, Crozier suggests that the addition of ARA be made in order to improve nerve tissue development, not to enhance weight gain. A person of ordinary skill, upon reading Crozier, would be discouraged from enhancing the weight gain of preterm infants via DHA and ARA supplementation. Kyle and Schweikhardt do not add any teaching that would suggest otherwise. Therefore, the combined teachings of Kyle, Crozier and Schweikhardt, taken as a whole (*i.e.*, that DHA causes a decrease in growth in preterm infants), would lead one of ordinary skill in the art away from enhancing the weight gain of preterm infants. As a result, the claimed method is patentably distinct over the combination of Kyle, Crozier and Schweikhardt.

Such a teaching away by Crozier must be considered by the Examiner as evidence of non-obviousness because a prior art reference must be considered in its entirety, including portions that would lead away from Applicant's claimed invention. See W.L. Gore & Associates, Inc. v. Garlock, Inc., 220 USPQ 303 (Fed. Cir. 1983). Specifically, the requirement of enhancing weight gain occurs not only in the preamble of Applicants' claim 1, but also in its body, which recites a weight gain enhancing amount of DHA and ARA. Applicants respectfully submit that these terms must be given patentable weight and that, by doing so, the claimed method is patentably distinct over the combination of references cited by the Examiner.

Regarding the establishment of unexpected results, the Examiner points out that it is Applicant's burden to explain any proffered data and establish how the results are unexpected and significant. The Examiner also points out that the claims must be commensurate in scope with any evidence of unexpected results. Lastly, the Examiner

asserts that the Applicant must compare the claimed subject matter with the closest prior art in order to be effective to rebut a case of obviousness.

Applicant submits that it has previously met its burden to explain the data and establish how the results are unexpected and significant. Applicant's unexpected results are illustrated by the data presented in the specification. Table 3 (page 28) shows the mean weight gains for preterm infants, with weight gains of 30.7 grams/day (g/d) for the Control group and 34.7 g/d for the DHA+ARA group. Table 5 also clearly demonstrates a significant difference in weight gain between the control and DHA+ARA fed groups. This is also illustrated in Figure 1, which is a graphical representation of the weight gain results between the DHA+ARA and Control groups. Further, at page 23, lines 7-13 of the Application, Applicants report the results as follows:

Post-hoc analysis reveals that infants on DA [DHA & ARA-enhanced formula] grew faster than infants receiving C [regular formula] and D [DHA-enhanced formula] (See table 5 and figure 1). This enhanced growth provided faster "premature infant catch-up" compared to C and D. Weight achieved by the DA group (3198 g) was higher than C (3075 g) and D (3051 g) at 40 weeks post-conceptual age but had not fully caught up to the term weight (3438 g) of group H [breast-fed term infants] (See table 4 and figure 2). This catch up trend continued through 48 to 57 weeks by which time the mean weight of group DA did not differ from group H while groups C and D remained significantly lower. (Emphasis added).

When compared to Crozier as the closest prior art, the results of the present invention are completely unexpected. Crozier fails to teach or suggest that enhancing the weight gain of preterm infants would be beneficial. In addition, Crozier fails to suggest that it is even possible to enhance the weight gain of preterm infants by the administration of DHA and ARA. The Examiner asserts that there is no comparison data showing how and why the data provided in the present invention is unexpected

and significant. Applicant has not shown any comparison data with Crozier because Crozier does not provide any data regarding these parameters.

Crozier does however, cite a study by Carlson, in which preterm infants given supplemental DHA actually demonstrated a decrease in weight gain. Carlson, *et al.*, *Effect of Long-Chain n-3 Fatty Acid Supplementation on Visual Acuity and Growth of Preterm Infants with and without Bronchopulmonary Dysplasia*, Am. J. Clin. Nutr. 63:687-97 (1996). This reference is more closely related to the invention than the art cited by the Examiner, and may be compared to the present invention instead. MPEP 716.02(e). In Carlson, absolute growth measurements showed that DHA-supplemented preterm infants weighed significantly less than standard formula-fed preterms at 2, 9 and 12 months and had smaller head circumferences at 9 months. Carlson, Am. J. Clin. Nutr. 63 at 692. The absolute growth measurements are shown in Table 6, on page 694. Carlson also notes that “[i]n the only other trial designed to study the effects of n-3 LCFA supplementation on growth, supplemented infants grew less well than infants fed commercially available formulas.” *Id.* (citing Carlson, *et al.*, *First Year Growth of Preterm Infants Fed Standard Compared to Marine Oil n-3 Supplemented Formula*, Lipids 27:901-07 (1992)).

Based on the results of Carlson, upon which Crozier relies, it is clear that any increase in weight gain due to DHA and ARA supplementation would be surprising and unexpected. Crozier does not suggest the benefit of the claimed invention, as asserted by the Examiner. Crozier nor any other reference discloses any range of enhanced weight gain due to DHA and ARA supplementation. Thus, the present invention is an unexpected result in kind, not merely in degree. Applicant’s specification contains

specific data indicating substantially improved results over the prior art and points out that the results were unexpected and surprising. This should suffice to establish unexpected results. *In re Soni*, 54 F.3d 746, 751 (Fed. Cir. 1995).

Applicant additionally asserts that the amended claims of the present invention are commensurate in scope with the evidence of unexpected results. The amended claims disclose a method for enhancing the weight gain of preterm infants by administering to them a weight gain enhancing amount of DHA and ARA. The experimental data in the application demonstrates an enhanced weight gain as a result of the administration of DHA and ARA. Thus, the scope of the amended claims are commensurate in scope with the evidence of unexpected results.

In summary, in view of the foregoing arguments and amendments, Applicants respectfully submit that claims 1-5, 14-17, and 21-22 are patentably distinct over the references cited by the Examiner and meet all other statutory requirements. Applicants believe that the present Application is now in complete condition for allowance and, therefore, respectfully request the Examiner to reconsider the rejections in the Office Action and allow this Application. The Examiner is invited to telephone the undersigned should any issues remain after the consideration of this response.

Please charge any additional fees that may be required to Deposit Account No.
50-2548.

Respectfully requested,

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March 17, 2005
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